Thonsgaard, 2022

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Circulating Concentrations of C-Type Natriuretic Peptides Increase with Sacubitril/Valsartan Treatment in Healthy Young Men. BACKGROUND C-type natriuretic peptide (CNP) is a cardioprotective peptide with high affinity for the ectoenzyme neutral endopeptidase (neprilysin). We aimed to determine whether angiotensin receptor-neprilysin inhibitor treatment acutely affects circulating concentrations of bioactive CNP and its molecular amino-terminal precursor (NT-proCNP). METHODS We included 9 and 10 healthy young men in 2 randomized crossover trials with <u>sacubitril</u>/valsartan vs control (Trial 1) and <u>sacubitril</u>/valsartan and sitagliptin vs sitagliptin (Trial 2). The participants were randomized to a single dose of <u>sacubitril</u>/valsartan (194/206 mg) or control at the first visit 30 min prior to a standardized meal intake. We obtained blood samples at 12 time points over 5 h and measured plasma concentrations of NT-proCNP in both trials and CNP in Trial 2. RESULTS NT-proCNP concentrations increased 3.5 h after <u>sacubitril/valsartan</u> treatment, and at 4.5 h concentrations were 42% and 65% higher compared with control in Trial 1 and Trial 2, respectively. The total area under the curve (tAUC)15-270 min was 22% higher (P = 0.007) in Trial 1 and 17% higher with treatment (P = 0.017) in Trial 2. Concentrations of bioactive CNP followed a similar temporal pattern with an increase of 93% at 4.5 h and a 31% higher tAUC15-270 min compared with control (P = 0.001) in Trial 2. CONCLUSIONS <u>Sacubitril</u>/valsartan augments circulating concentrations of both bioactive CNP and NT-proCNP in healthy young men. The increase in bioactive CNP is most likely caused by de novo synthesis and secretion rather than diminished breakdown through neprilysin inhibition.ClinicalTrials.gov registration number NCT03717688.

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